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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,101	03/05/2002	Jean-Marc Zuccarelli	C1190/20007	2827

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EXAMINER
YOUNG, MICAH PAUL

ART UNIT	PAPER NUMBER
1615	11

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,101	ZUCCARELLI ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Acknowledgment of Papers Received: Amendment and Response dated 3/31/03.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 10 – 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carli et al (USPN 5,275,824) and Dunn et al (USPN 4,308,251) in view of Ghanta et al (USPN 5,814,332). Claims 10 – 16 are drawn to ibuprofen particles that are coated with cellulose derivatives and colloidal silica. The claims recite specific concentrations of each coating component in relation to the ibuprofen, and the other components. The particles further include other excipients including surfactants, alkali metals, glycerides, and starches. Claims 17 – 22 are drawn to a process of making the particles where the pH is maintained by a buffer and a particular level, while the temperature of the drug is maintained below 35 degrees Celsius. The process recites that the particles are below 100 microns. The claims also recite that the granulation and coating occur at the same time.

Carli et al teaches a dosage form comprising granules of ibuprofen coated in cellulose derivatives and colloidal silica. The cellulose derivatives are selected from ethyl cellulose, hydroxypropylcellulose and methylcellulose, and mixtures and combination thereof (col. 4, lin.

65 – 67). The particles are wet granulated in a conventional solvent, and range in size from 10 – 1000 microns (col. 2, lin. 55 – 57). The coating can further include other polymers, which are added to the mixture along with Aerosil, a silica product (Examples). Also the temperature of the product of the reference ranges from 20 – 25 degrees Celsius. The reference however does not specify what type of solvent is used, and does not specify a particular pH requirement but specifies that it can be modified by addition components. The reference also does not disclose the specific ranges and concentrations as claimed by applicant.

Dunn et al teaches dosage form comprising coated granules of ibuprofen. The granules are coated with cellulose derivatives and a silica product. The cellulose derivatives are selected from methylcellulose, hydroxypropylmethylcellulose, ethyl cellulose and other derivatives (claim 1). The particles are wet granulated with an alcoholic solvent (col. 5, lin. 42 – 51). Other excipients are added to the granule mixture including starches and other cellulose derivatives. The pH of the solution is maintained by a buffer at 7.5, yet can be modified to suit the needs of the dosage form (Examples). The reference also includes Aerosil in the coating of the granules.

Both references provide the theory to the coating of granulated ibuprofen with cellulose derivatives and silica products, yet the references are silent to the order in which they happen. Whether the granulation is first of the particles are coated and then granulated. Ghanta et al teaches a method for making coated granules of NSAID drugs and controlling the pH. The granules are coated with a cellulose derivative, and a colloidal silicone product. The reference teaches that the granulation and coating of the NSAID drug occur simultaneously (col. 3, lin. 44 – 60). Throughout the process the temperature of the product remains below 40 degrees and

drops as low as 10 degrees Celsius. The reference also discloses that other excipients are included such as mannitol (Example).

With regard to the applicant's limitation that the granules include ibuprofen, its isomers and pharmaceutical salts thereof, it is the position of the examiner that these compounds are obvious variants of one another. It is obvious to a skilled artisan to include pharmaceutical salts of an active agent in order to improve the bioavailability. Isomers of a compound are simply obvious variants, rearrangements of the original compound.

With regard to the ranges and concentrations recited by applicant, it is the position of the examiner that these limitations are merely recitations of the optimal workable ranges and do not impart patentability. The art presents the general theory of coating ibuprofen granules with cellulose derivatives and a silica product. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *See* In re Aller, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various cosmetic compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *See* In re Russell, 439 F.2d 1228 169 USPQ 426 (CCPA 1971).

With these aspects in mind, one of ordinary in the art would be motivated to follow the teachings and suggestions in the art. Ghanta provides the theory of simultaneously granulating and coating ibuprofen particles with cellulose derivatives, silica products. A skilled artisan

would have taken this theory and applied the components of either Carli or Dunn to produce coated granules, which could be formulated into compressed tablets with improved bioavailability. A skilled artisan would be able to maintain the pH of the product at a level suitable for the best application of the granules, dependent upon the administration. It would have been obvious to one of ordinary skill in the art to combine these teaches and suggestions with an expected result of micronized granule capable of being compressed into tablets with improved bioavailability.

Response to Arguments

3. Applicant's arguments filed 3/18/03 have been fully considered but they are not persuasive. Applicant argues that:

a. Carli does not describe coated granules of ibuprofen for immediate release,

b. Dunn does not disclose the invention and teaches away from the invention,

c. Ghanta teaches away form the invention.

4. With regard to argument a., b. and c., it is the position of the examiner that both references suggest coated ibuprofen or equivalent agents. The coatings of theses references comprise cellulose derivatives, (ethyl cellulose, hydroxymethylcellulose, and colloidal silicone). Carli disclose the particles as nanoparticles, while the particles of applicant are micro-particles. Applicant is reminded that nanoparticles are merely smaller micro-particles. The claims require that the particles be coated with ethyl cellulose, hydroxypropyl cellulose and a silicone product. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the physico-chemical integrity of the particles) are not recited in the rejected claim(s). Although the claims are

interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In fact the references are used for their disclosures of coated ibuprofen, not for their process, though they are processed through wet granulation in alcoholic solvents. Dunn is used to show the theory of simultaneously granulating and coating NSAID agents with cellulose derivatives and silicon products. The theory can be applied to the ingredients of Carli or Dunn, and a skilled artisan would expect similar results since the procedure of Dunn requires similar components. Dunn was not used to its components but rather the suggestion of cellulose derivatives, NSAIDs and silicon. Also, applicant argues that since Dunn includes hardening agents, the reference teaches away from the invention. In fact, applicant's claims are written with open claim language that does not exclude hardening agents from the formulation. Further the process of Dunn is done simultaneously, and keeps the temperature of the ibuprofen under 35 degrees. These features of the invention are within the limits of the claims and would be obvious to a skilled artisan.

5. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 703-308-7005. The examiner can normally be reached on M-F 7:30am - 4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-7648 for regular communications and 703-746-7648 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Micah-Paul Young
Examiner
Art Unit 1615

MP Young
June 1, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600